β1α1

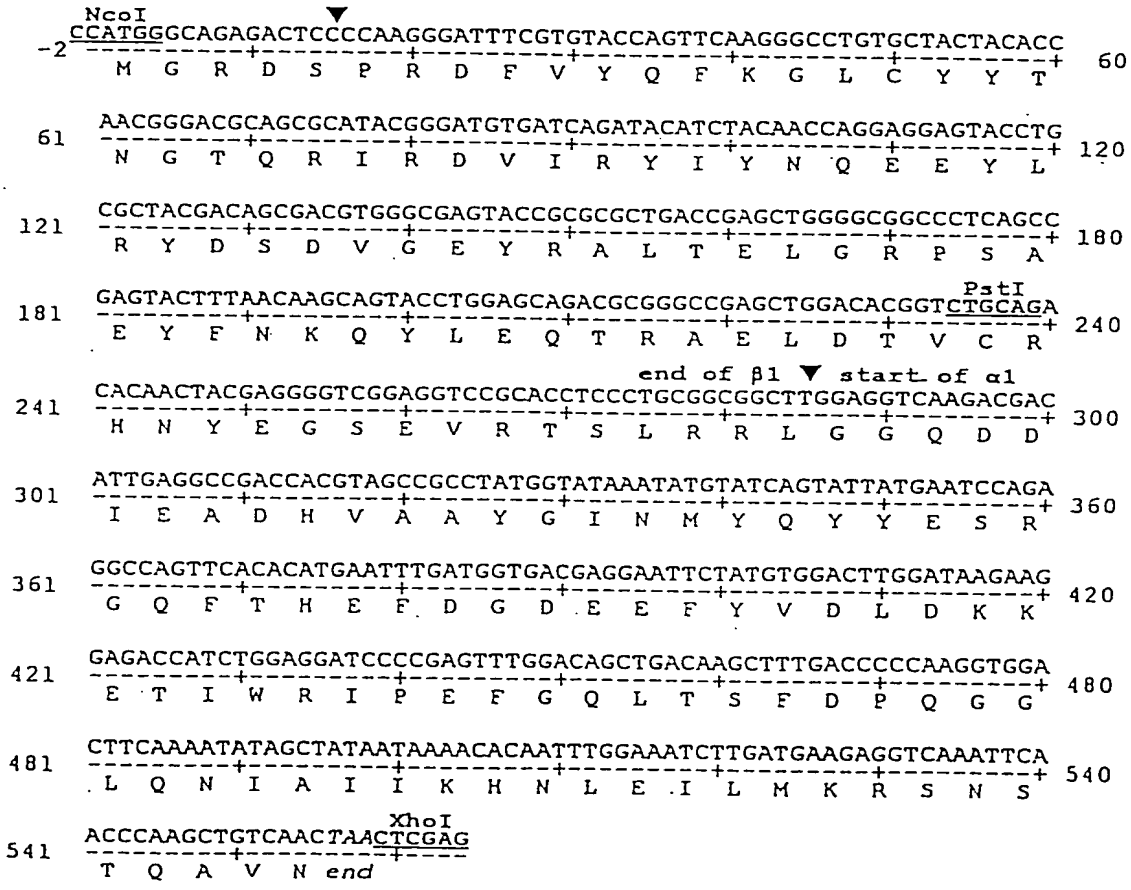

NcoI
CCATGGGCAGAGACTCCCCAAGGGATTTCGTGTACCAGTTCAAGGGCCTGTGCTACTACACC
-2 M G R D S P R D F V Y Q F K G L C Y Y T 60
AACGGGACGCAGCGCATACGGGATGTGATCAGATACATCTACAACCAGGAGGAGTACCTG
61 N G T Q R I R D V I R Y I Y N Q E E Y L 120
CGCTACGACAGCGACGTGGGCGAGTACCGCGCGCTGACCGAGCTGGGGCGGCCCTCAGCC
121 R Y D S D V G E Y R A L T E L G R P S A 180
PstI
GAGTACTTTAACAAGCAGTACCTGGAGCAGACGCGGGCCGAGCTGGACACGGTCTGCAGA
181 E Y F N K Q Y L E Q T R A E L D T V C R 240
end of β1 ▼ start of α1
CACAACTACGAGGGGTCGGAGGTCCGCACCTCCCTGCGGCGGCTTGGAGGTCAAGACGAC
241 H N Y E G S E V R T S L R R L G G Q D D 300
ATTGAGGCCGACCACGTAGCCGCCTATGGTATAAATATGTATCAGTATTATGAATCCAGA
301 I E A D H V A A Y G I N M Y Q Y Y E S R 360
GGCCAGTTCACACATGAATTTGATGGTGACGAGGAATTCTATGTGGACTTGGATAAGAAG
361 G Q F T H E F D G D E E F Y V D L D K K 420
GAGACCATCTGGAGGATCCCCGAGTTTGGACAGCTGACAAGCTTTGACCCCCAAGGTGGA
421 E T I W R I P E F G Q L T S F D P Q G G 480
CTTCAAAATATAGCTATAATAAAACACAATTTGGAAATCTTGATGAAGAGGTCAAATTCA
481 L Q N I A I I K H N L E I L M K R S N S 540
XhoI
ACCCAAGCTGTCAACTAACTCGAG
541 T Q A V N end

FIG. 1A

FIG. 1B

β1α1/MBP-72-89

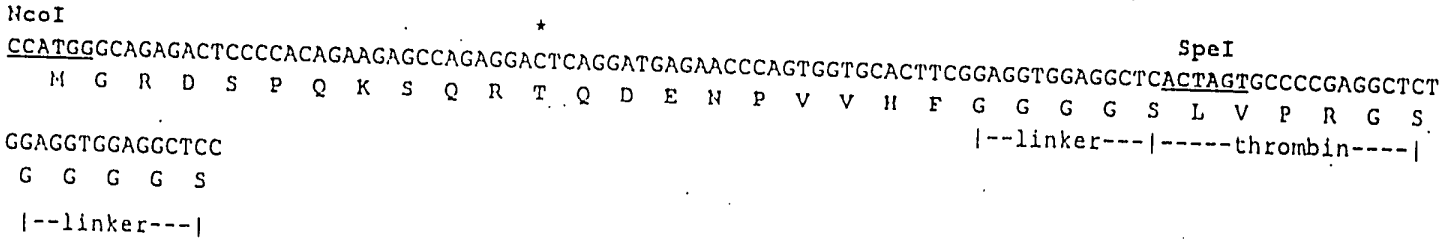


FIG. 1C

β1α1/MBP-55-69

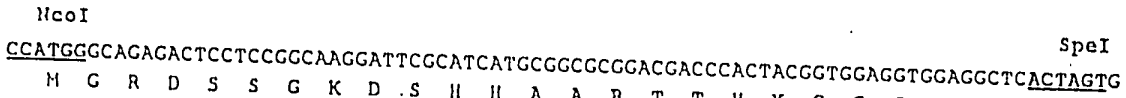
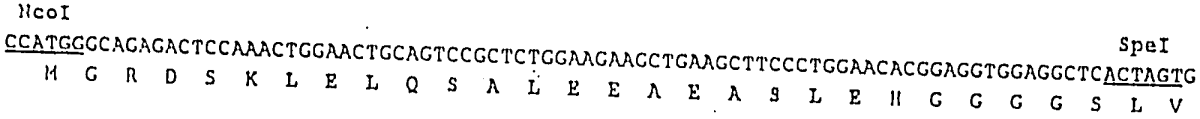
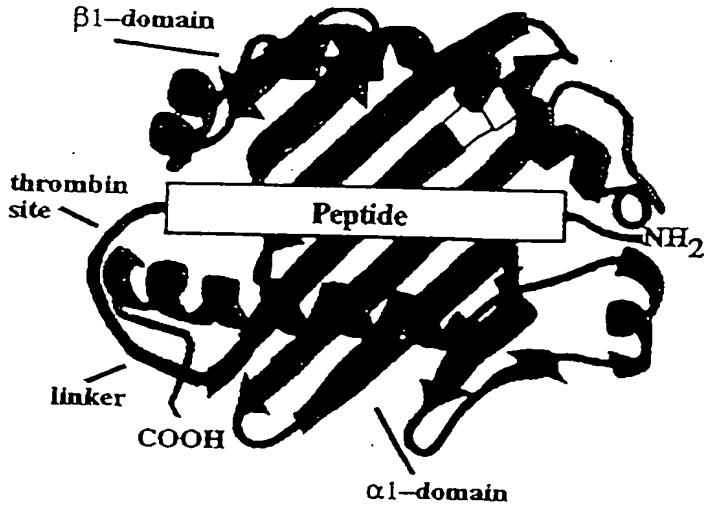


FIG. 1D

β1α1/CM-2



a. RT1.B



b. β1α1/peptide

FIG. 2
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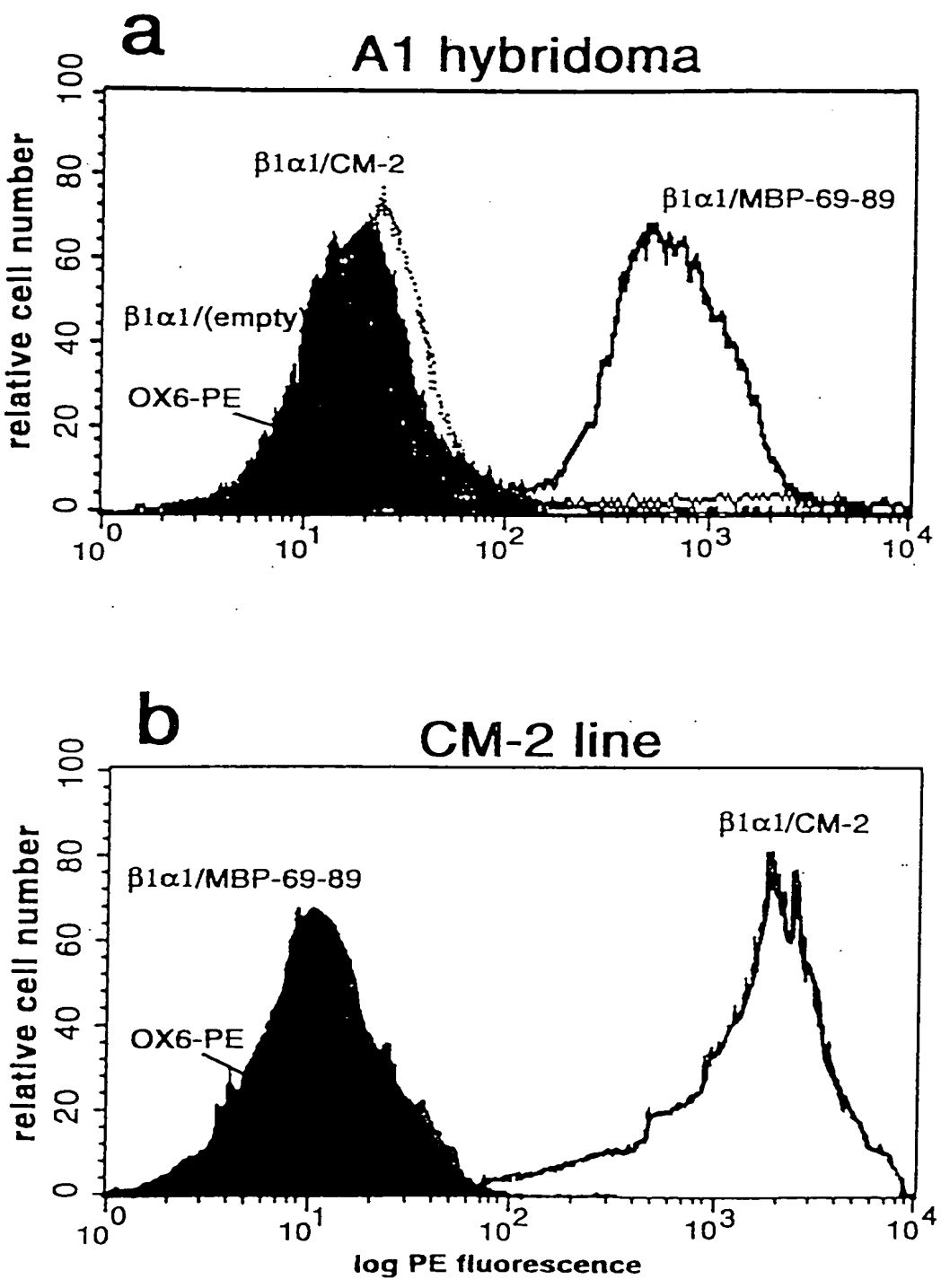
a
A1 hybridoma
relative cell number
β1α1/CM-2
β1α1/MBP-69-89
β1α1/(empty)
OX6-PE
b
CM-2 line
β1α1/CM-2
β1α1/MBP-69-89
OX6-PE
log PE fluorescence

FIG. 3

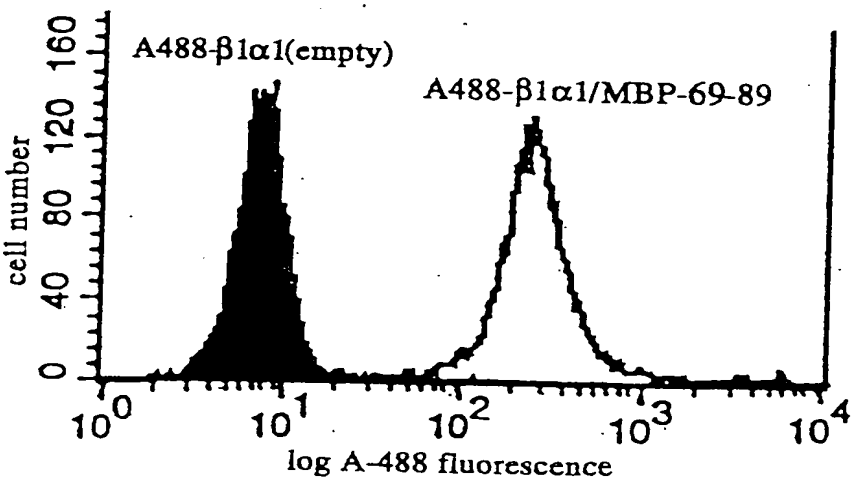
A488-β1α1(empty)
A488-β1α1/MBP-69-89
cell number
0
40
80
120
160
10^0
10^1
10^2
10^3
10^4
log A-488 fluorescence

FIG. 4
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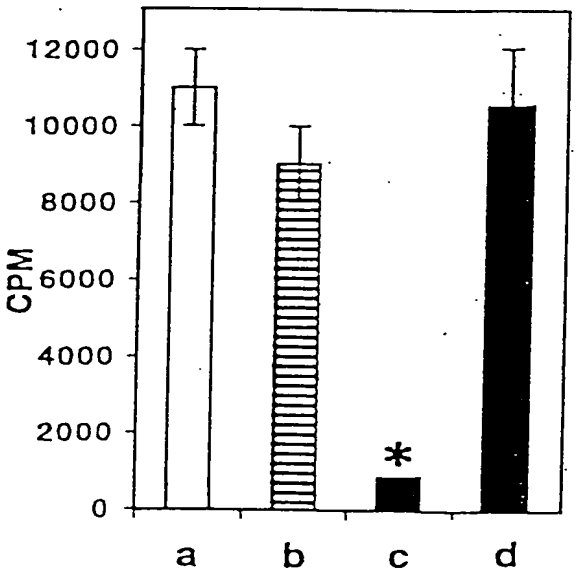
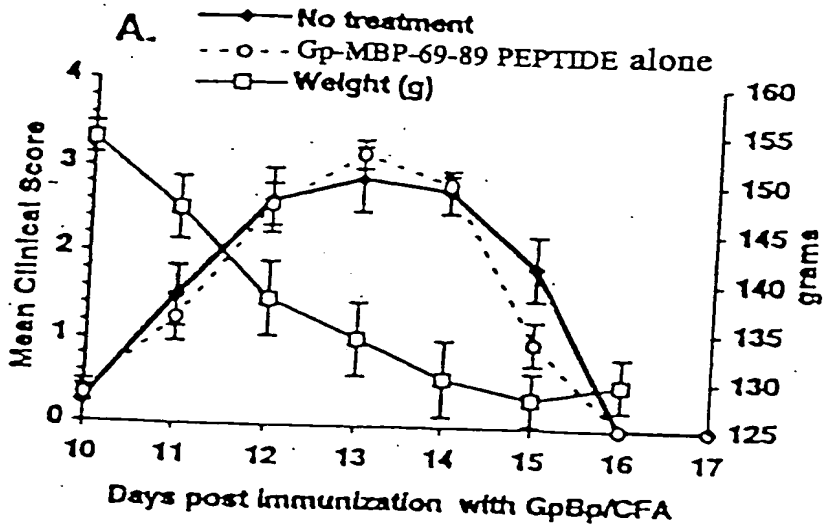


FIG. 5


A.
No treatment
Gp-MBP-69-89 PEPTIDE alone
Weight (g)
Mean Clinical Score
grams
Days post immunization with GpBp/CFA

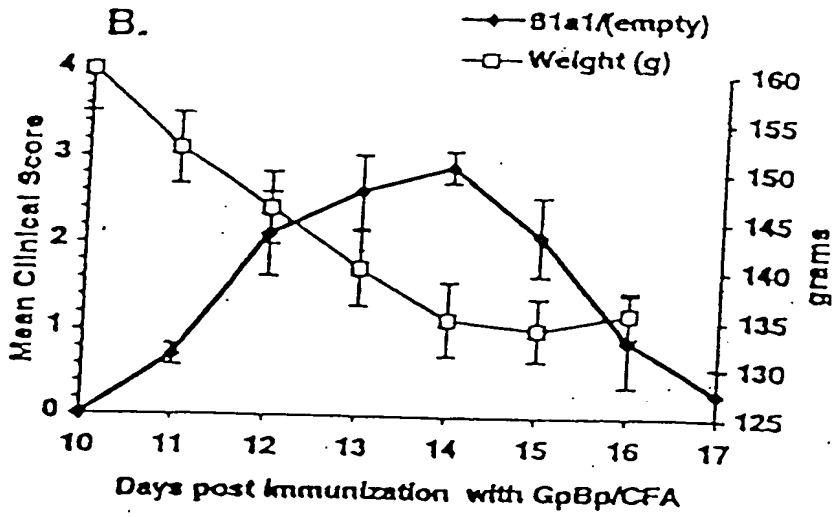
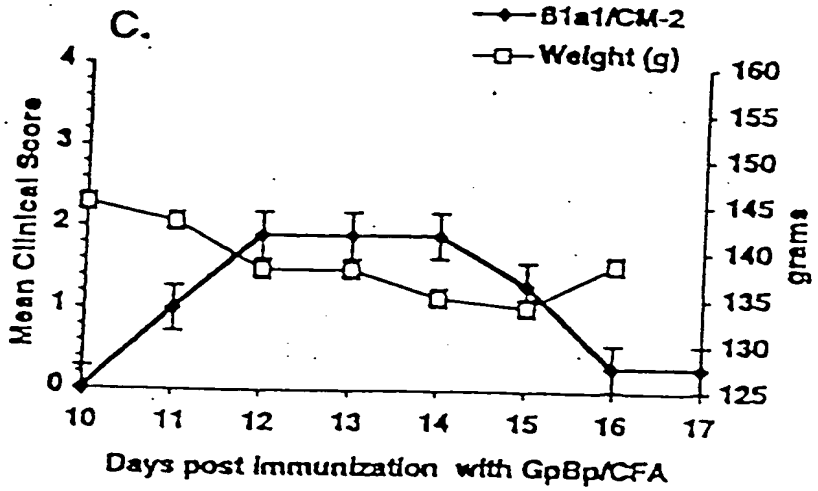

B.
B1a1/(empty)
Weight (g)
Mean Clinical Score
grams
Days post immunization with GpBp/CFA

FIG. 6A


C.
B1a1/CM-2
Weight (g)
Mean Clinical Score
grams
Days post immunization with GpBp/CFA

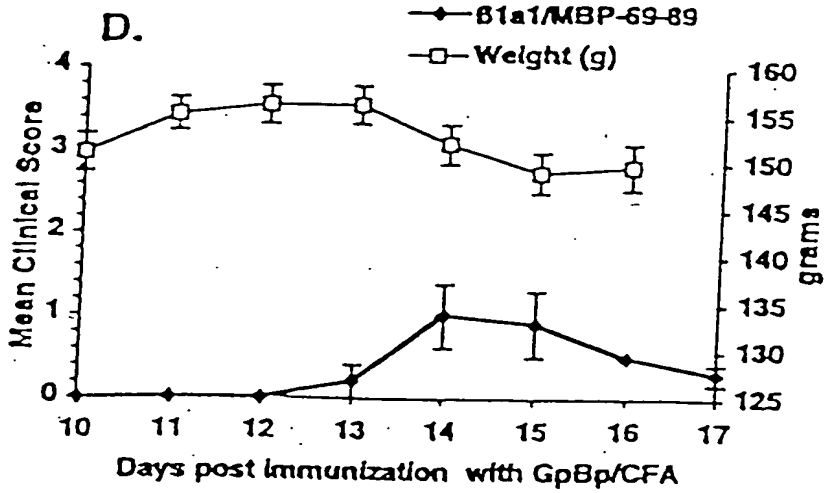

D.
B1a1/MBP-69-89
Weight (g)
Mean Clinical Score
grams
Days post immunization with GpBp/CFA

FIG. 6B

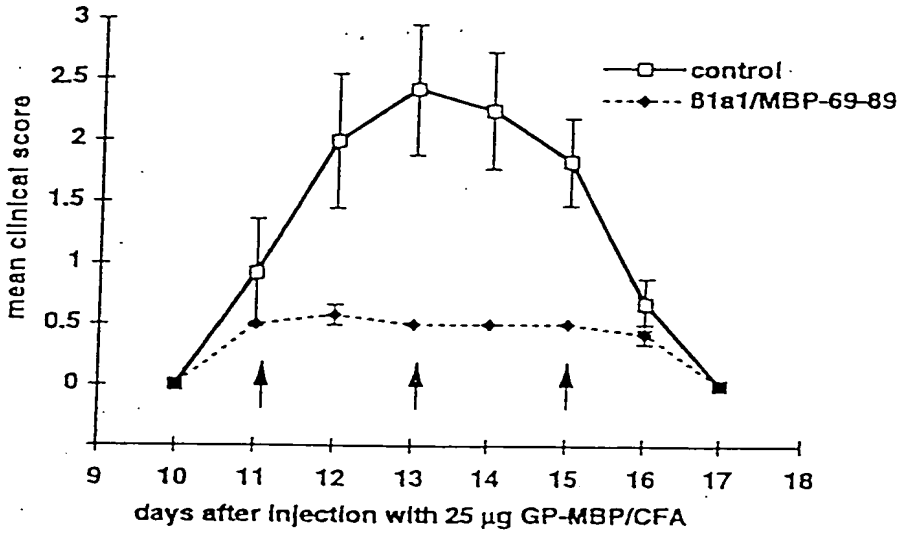

mean clinical score
3
2.5
2
1.5
1
0.5
0
9
10
11
12
13
14
15
16
17
18
days after injection with 25 µg GP-MBP/CFA
control
81a1/MBP-69-89

FIG. 7

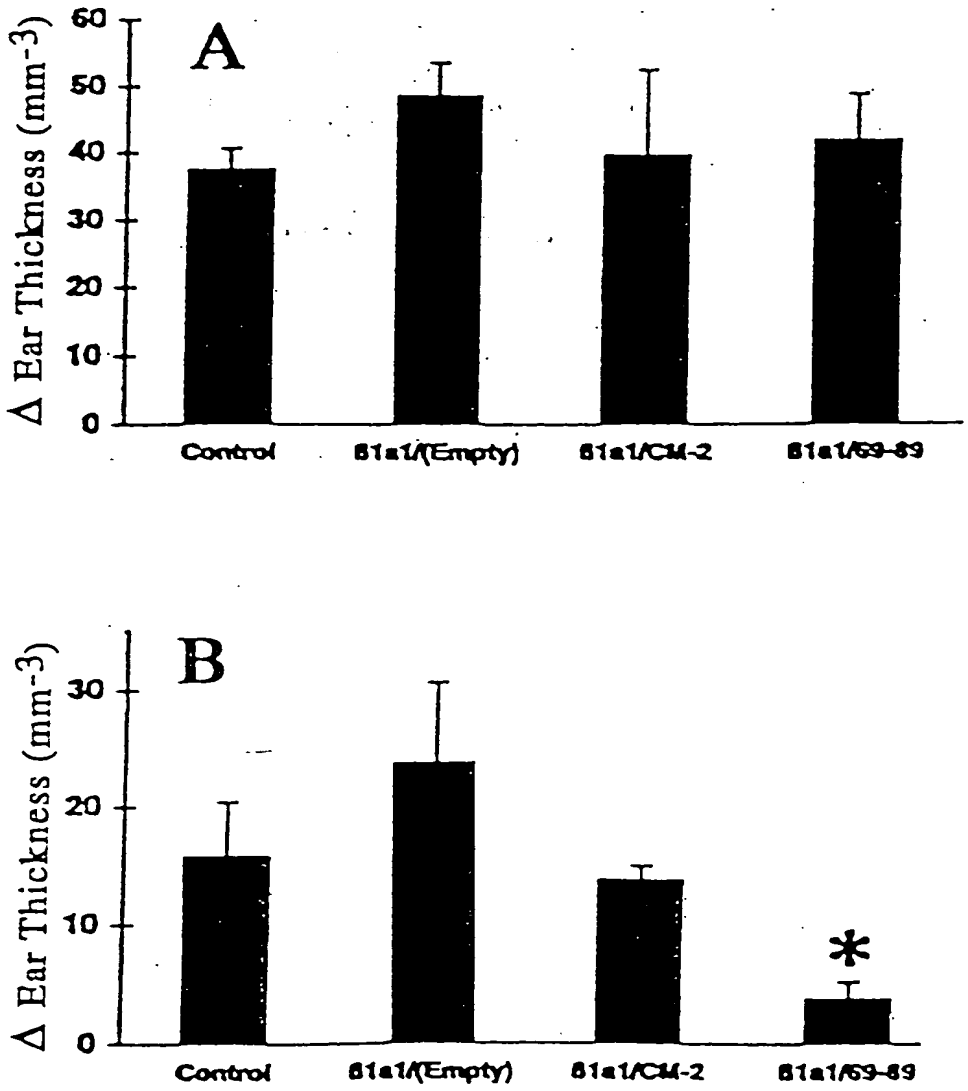

A
Δ Ear Thickness (mm-3)
60
50
40
30
20
10
0
Control
B1a1/(Empty)
B1a1/CM-2
B1a1/69-89
B
Δ Ear Thickness (mm-3)
30
20
10
0
*
Control
B1a1/(Empty)
B1a1/CM-2
B1a1/69-89

FIG. 8

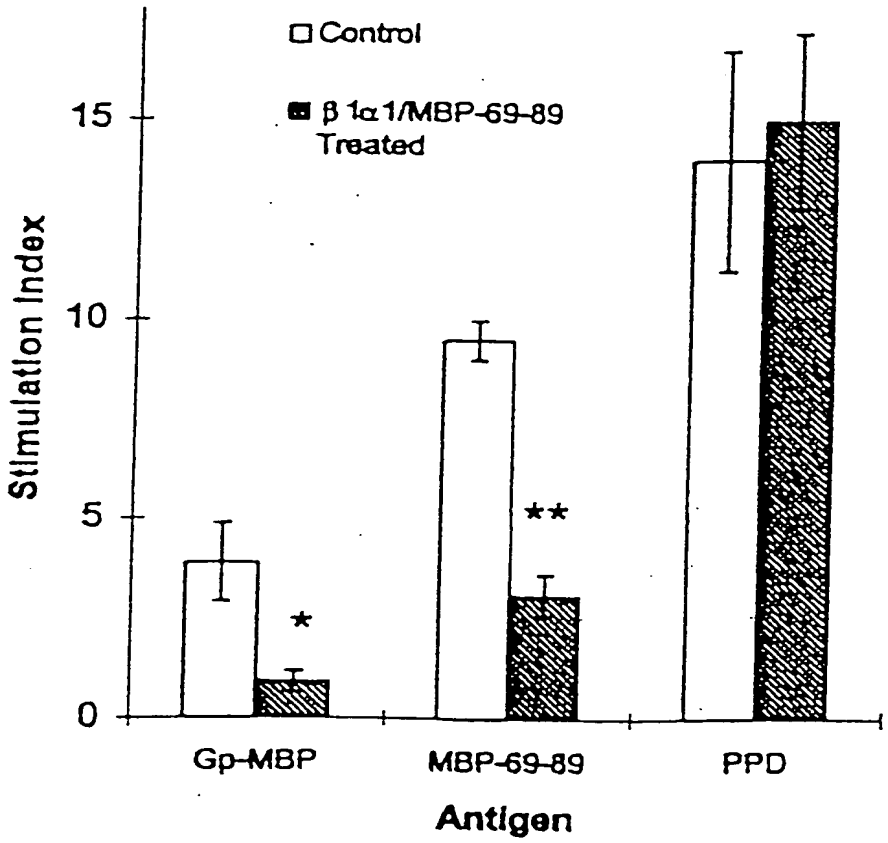

Control
β 1α1/MBP-69-89
Treated
Stimulation Index
15
10
5
0
*
**
Gp-MBP
MBP-69-89
PPD
Antigen

FIG. 9

β1 domain:
ARG4-PRO5-ARG6-PHE7-LEU8-TRP9-GLN10-LEU11-LYS12-PHE13-GLU14-CYS15-
HIS16-PHE17-PHE18-ASN19-GLY20-THR21-GLU22-ARG23-VAL24-ARG25-LEU26-
LEU27-GLU28-ARG29-CYS30-ILE31-TYR32-ASN33-GLN34-GLU35-GLU36-SER37-
VAL38-ARG39-PHE40-ASP41-SER42-ASP43-VAL44-GLY45-GLU46-TYR47-ARG48-
ALA49-VAL50-THR51-GLU52-LEU53-GLY54-ARG55-PRO56-ASP57-ALA58-GLU59-
TYR60-TRP61-ASN62-SER63-GLN64-LYS65-ASP66-LEU67-LEU68-GLU69-GLN70-
ARG71-ARG72-ALA73-ALA74-VAL75-ASP76-THR77-TYR78-CYS79-ARG80-HIS81-
ASN82-TYR83-GLY84-VAL85-GLY86-GLU87-SER88-PHE89-THR90-VAL91-GLN92-
ARG93-ARG94-VAL95
α1 domain:
GLU3-GLU4-HIS5-VAL6-ILE7-ILE8-GLN9-ALA10-GLU11-PHE12-TYR13-LEU14-
ASN15-PRO16-ASP17-GLN18-SER19-GLY20-GLU21-PHE22-MET23-PHE24-ASP25-
PHE26-ASP27-GLY28-ASP29-GLU30-ILE31-PHE32-HIS33-VAL34-ASP35-MET36-
ALA37-LYS38-LYS39-GLU40-THR41-VAL42-TRP43-ARG44-LEU45-GLU46-GLU47-
PHE48-GLY49-ARG50-PHE51-ALA52-SER53-PHE54-GLU55-ALA56-GLN57-GLY58-
ALA59-LEU60-ALA61-ASN62-ILE63-ALA64-VAL65-ASP66-LYS67-ALA68-ASN69-
LEU70-GLU71-ILE72-MET73-THR74-LYS75-ARG76-SER77-ASN78-TYR79-THR80-
PRO81-ILE82-THR83-ASN84

FIG. 10A
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β1 domain:
ARG4-PRO5-TRP6-PHE7-LEU8-GLU9-TYR10-CYS11-LYS12-SER13-GLU14-CYS15-
HIS16-PHE17-TYR18-ASN19-GLY20-THR21-GLN22-ARG23-VAL24-ARG25-LEU26-
LEU27-VAL28-ARG29-TYR30-PHE31-TYR32-ASN33-LEU34-GLU35-GLU36-ASN37-
LEU38-ARG39-PHE40-ASP41-SER42-ASP43-VAL44-GLY45-GLU46-PHE47-ARG48-
ALA49-VAL50-THR51-GLU52-LEU53-GLY54-ARG55-PRO56-ASP57-ALA58-GLU59-
ASN60-TRP61-ASN62-SER63-GLN64-PRO65-GLU66-PHE67-LEU68-GLU69-GLN70-
LYS71-ARG72-ALA73-GLU74-VAL75-ASP76-THR77-VAL78-CYS79-ARG80-HIS81-
ASN82-TYR83-GLU84-ILE85-PHE86-ASP87-ASN88-PHE89-LEU90-VAL91-PRO92-
ARG93-ARG94-VAL95

α1 domain:
GLU3-GLU4-HIS5-THR6-ILE7-ILE8-GLN9-ALA10-GLU11-PHE12-TYR13-LEU14-
LEU15-PRO16-ASP17-LYS18-ARG19-GLY20-GLU21-PHE22-MET23-PHE24-ASP25-
PHE26-ASP27-GLY28-ASP29-GLU30-ILE31-PHE32-HIS33-VAL34-ASP35-ILE36-
GLU37-LYS38-SER39-GLU40-THR41-ILE42-TRP43-ARG44-LEU45-GLU46-GLU47-
PHE48-ALA49-LYS50-PHE51-ALA52-SER53-PHE54-GLU55-ALA56-GLN57-GLY58-
ALA59-LEU60-ALA61-ASN62-ILE63-ALA64-VAL65-ASP66-LYS67-ALA68-ASN69-
LEU70-ASP71-VAL72-MET73-LYS74-GLU75-ARG76-SER77-ASN78-ASN79-THR80-
PRO81-ASP82-ALA83-ASN84

FIG. 10B
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β1 domain:
MET(-2)-GLY(-1)-ARG1-ASP2-SER3-PRO4-ARG5-ASP6-PHE7-VAL8-TYR9-
GLN10-PHE11-LYS12-GLY13-LEU14-CYS15-TYR16-TYR17-THR18-ASN19-GLY20-
THR21-GLN22-ARG23-ILE24-ARG25-ASP26-VAL27-ILE28-ARG29-TYR30-ILE31-
TYR32-ASN33-GLN34-GLU35-GLU36-TYR37-LEU38-ARG39-TYR40-ASP41-SER42-
ASP43-VAL44-GLY45-GLU46-TYR47-ARG48-ALA49-LEU50-THR51-GLU52-LEU53-
GLY54-ARG55-PRO56-SER57-ALA58-GLU59-TYR60-TRP61-ASN62-SER63-GLN64-
LYS65-GLN66-TYR67-LEU68-GLU69-GLN70-THR71-ARG72-ALA73-GLU74-LEU75-
ASP76-THR77-VAL78-CYS79-ARG80-HIS81-ASN82-TYR83-GLU84-GLY85-SER86-
GLU87-VAL88-ARG89-THR90-SER91-LEU92-ARG93-ARG94-LEU95

α1 domain:
ALA2-ASP3-HIS4-VAL5-ALA6-ALA7-TYR8-GLY9-ILE10-ASN11-MET12-TYR13-
GLN14-TYR15-TYR16-GLU17-SER18-ARG19-GLY20-GLN21-PHE22-THR23-HIS24-
GLU25-PHE26-ASP27-GLY28-ASP29-GLU30-GLU31-PHE32-TYR33-VAL34-ASP35-
LEU36-ASP37-LYS38-LYS39-GLU40-THR41-ILE42-TRP43-ARG44-ILE45-PRO46-
GLU47-PHE48-GLY49-GLN50-LEU51-THR52-SER53-PHE54-ASP55-PRO56-GLN57-
GLY58-GLY59-LEU60-GLN61-ASN62-ILE63-ALA64-ILE65-ILE66-LYS67-HIS68-
ASN69-LEU70-GLU71-ILE72-LEU73-MET74-LYS75-ARG76-SER77-ASN78-SER79-
THR80-GLN81-ALA82-VAL83-ASN84

FIG. 10C
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α1 domain:
GLY1-SER2-HIS3-SER4-MET5-ARG6-TYR7-PHE8-TYR9-THR10-ALA11-MET12-
SER13-ARG14-PRO15-GLY16-ARG17-GLY18-GLU19-PRO20-ARG21-PHE22-ILE23-
ALA24-VAL25-GLY26-TYR27-VAL28-ASP29-ASP30-THR31-GLN32-PHE33-VAL34-
ARG35-PHE36-ASP37-SER38-ASP39-ALA40-ALA41-SER42-PRO43-ARG44-THR45-
GLU46-PRO47-ARG48-PRO49-PRO50-TRP51-ILE52-GLU53-GLN54-GLU55-GLY56-
PRO57-GLU58-TYR59-TRP60-ASP61-ARG62-ASN63-THR64-GLN65-ILE66-PHE67-
LYS68-THR69-ASN70-THR71-GLN72-THR73-TYR74-ARG75-GLU76-ASN77-LEU78-
ARG79-ILE80-ALA81-LEU82-ARG83-TYR84-

α2 domain:
TYR85-ASN86-GLN87-SER88-GLU89-ALA90-GLY91-SER92-HIS93-ILE94-ILE95-
GLN96-ARG97-MET98-TYR99-GLY100-CYS101-ASP102-LEU103-GLY104-PRO105-
ASP106-GLY107-ARG108-LEU109-LEU110-ARG111-GLY112-HIS113-ASP114-
GLN115-SER116-ALA117-TYR118-ASP119-GLY120-LYS121-ASP122-TYR123
ILE124-ALA125-LEU126-ASN127-GLU128-ASP129-LEU130-SER131-SER132-
TRP133-THR134-ALA135-ALA136-ASP137-THR138-ALA139-ALA140-GLN141-
ILE142-THR143-GLN144-ARG145-LYS146-TRP147-GLU148-ALA149-ALA150-
ARG151-VAL152-ALA153-GLU154-GLN155-LEU156-ARG157-ALA158-TYR159-
LEU160-GLU161-GLY162-LEU163-CYS164-VAL165-GLU166-TRP167-LEU168-
ARG169-ARG170-TYR171-LEU172-GLU173-ASN174-GLY175-LYS176-GLU177-
THR178-LEU179-GLN180-ARG181-ALA182-ASP183-PRO184

FIG. 11
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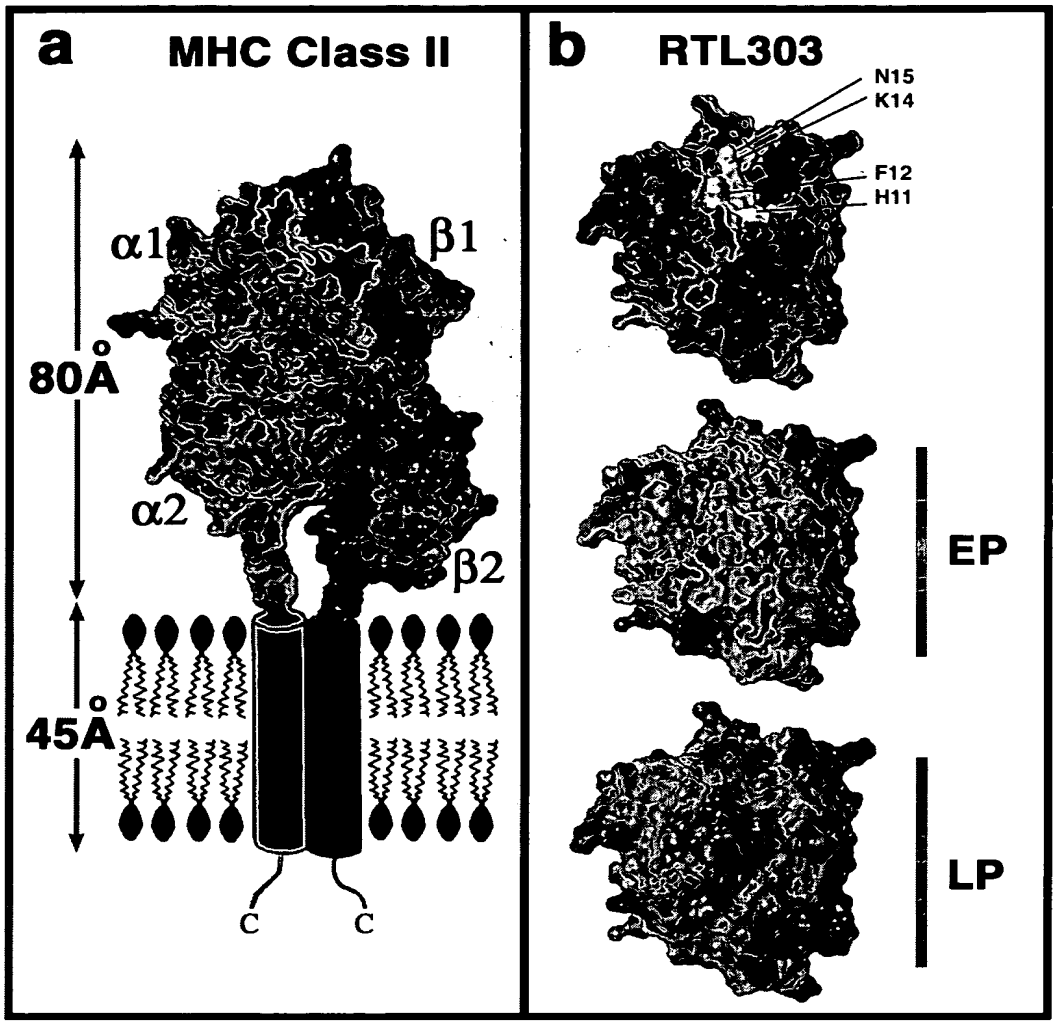
FIG. 12

FIG. 12


a
MHC Class II
α1
β1
80Å
α2
β2
45Å
C
C
b
RTL303
N15
K14
F12
H11
EP
LP

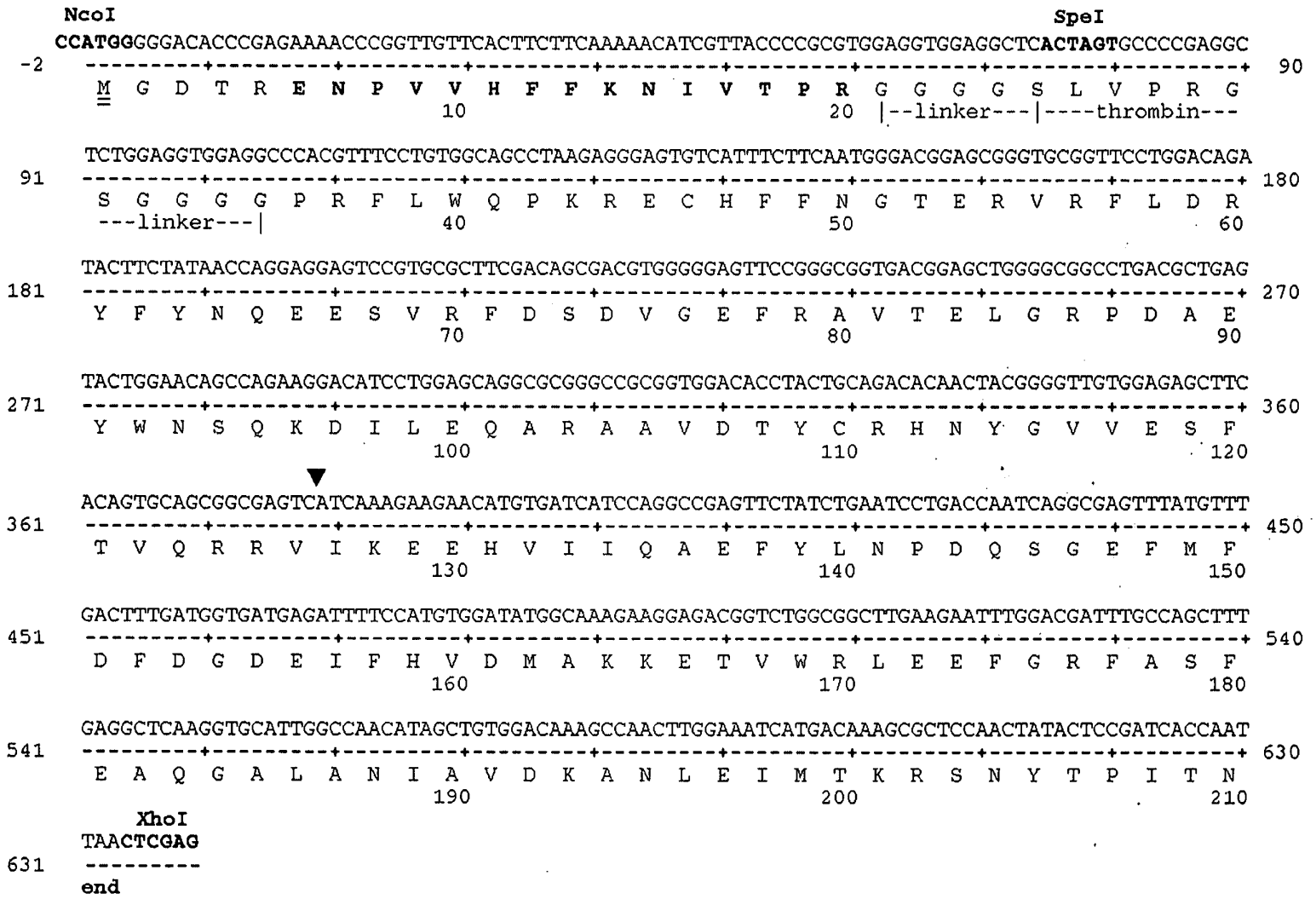


FIG. 13

FIG. 14

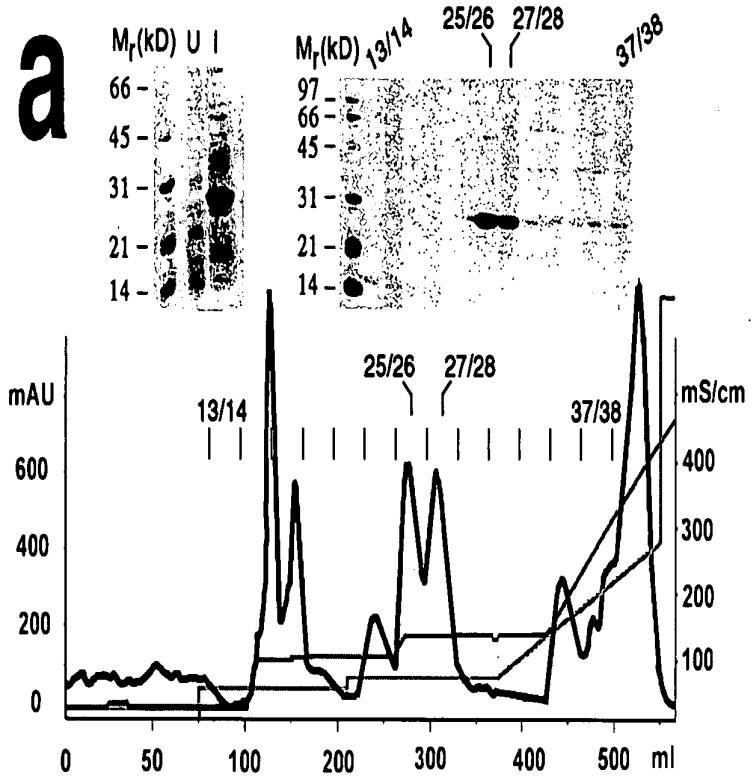
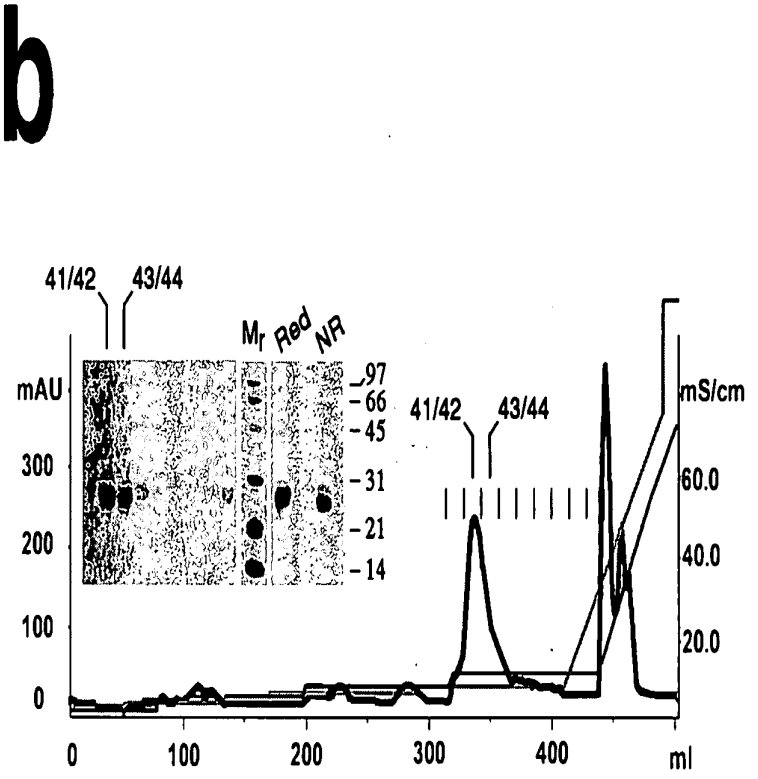

a
Mr(kD) U I
66
45
31
21
14
Mr(kD)
97
66
45
31
21
14
13/14
25/26
27/28
37/38
mAU
600
400
200
0
mS/cm
400
300
200
100
0
50
100
200
300
400
500
ml

FIG. 14


b
41/42
43/44
Mr Red NR
97
66
45
31
21
14
mAU
300
200
100
0
mS/cm
60.0
40.0
20.0
0
100
200
300
400
ml

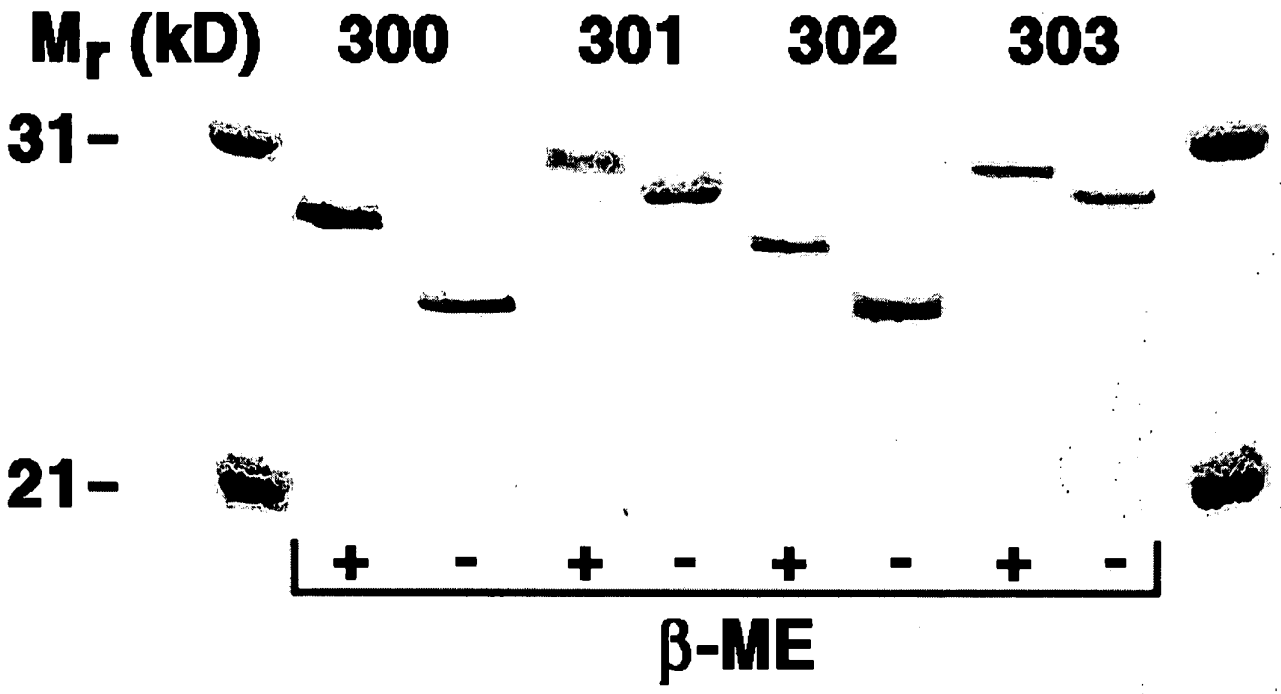


FIG. 15

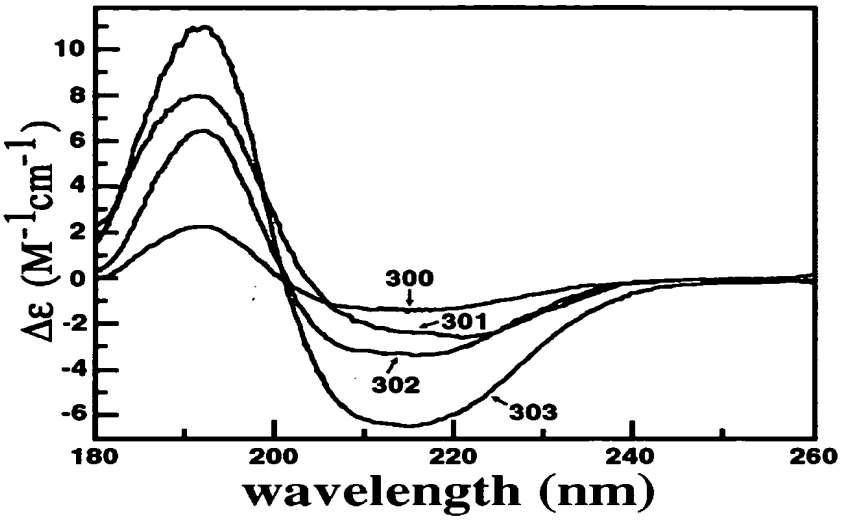

10
8
6
4
2
0
-2
-4
-6
Δε (M-1cm-1)
300
301
302
303
180
200
220
240
260
wavelength (nm)

FIG. 16

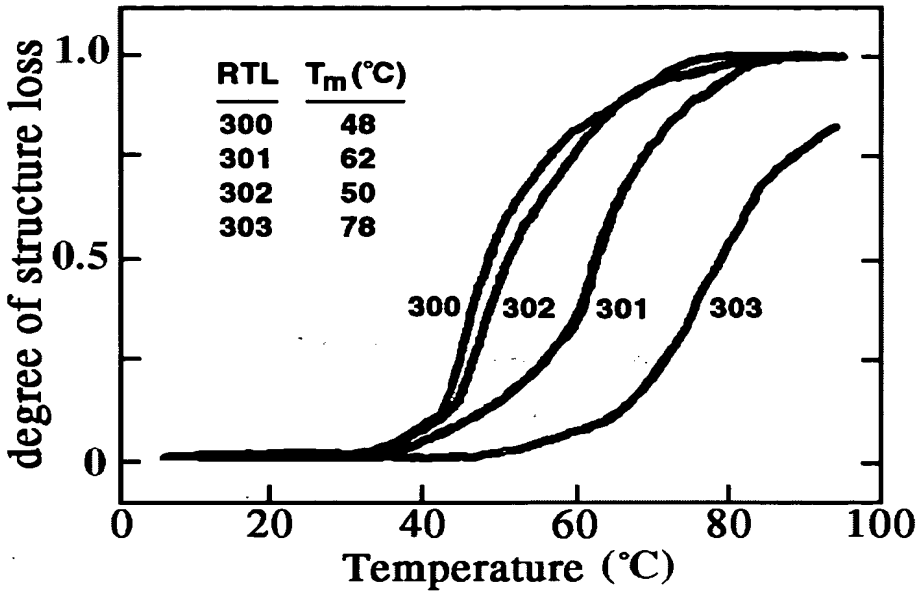

degree of structure loss
1.0
0.5
0
RTL
T_m(°C)
300
48
301
62
302
50
303
78
300
302
301
303
0
20
40
60
80
100
Temperature (°C)

FIG. 17

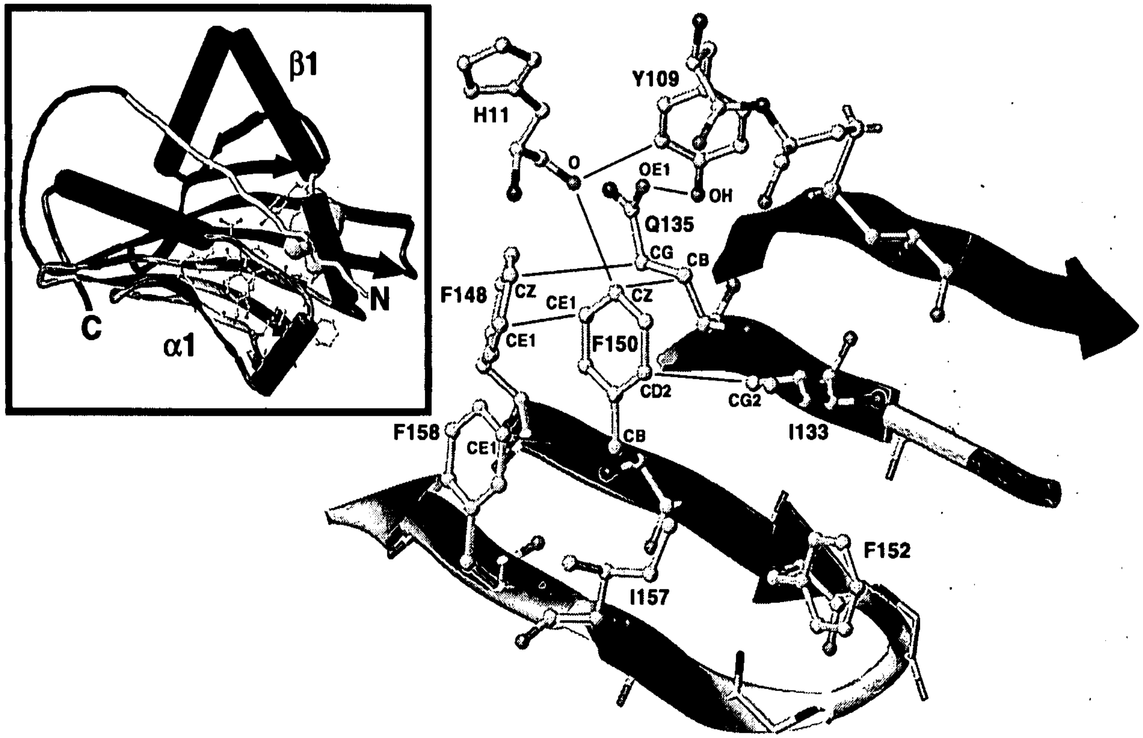

β1
N
C
α1
H11
Y109
O
OE1
OH
Q135
CG
CB
F148
CZ
CE1
CZ
F150
CE1
CD2
CG2
I133
F158
CE1
CB
F152
I157

FIG. 18

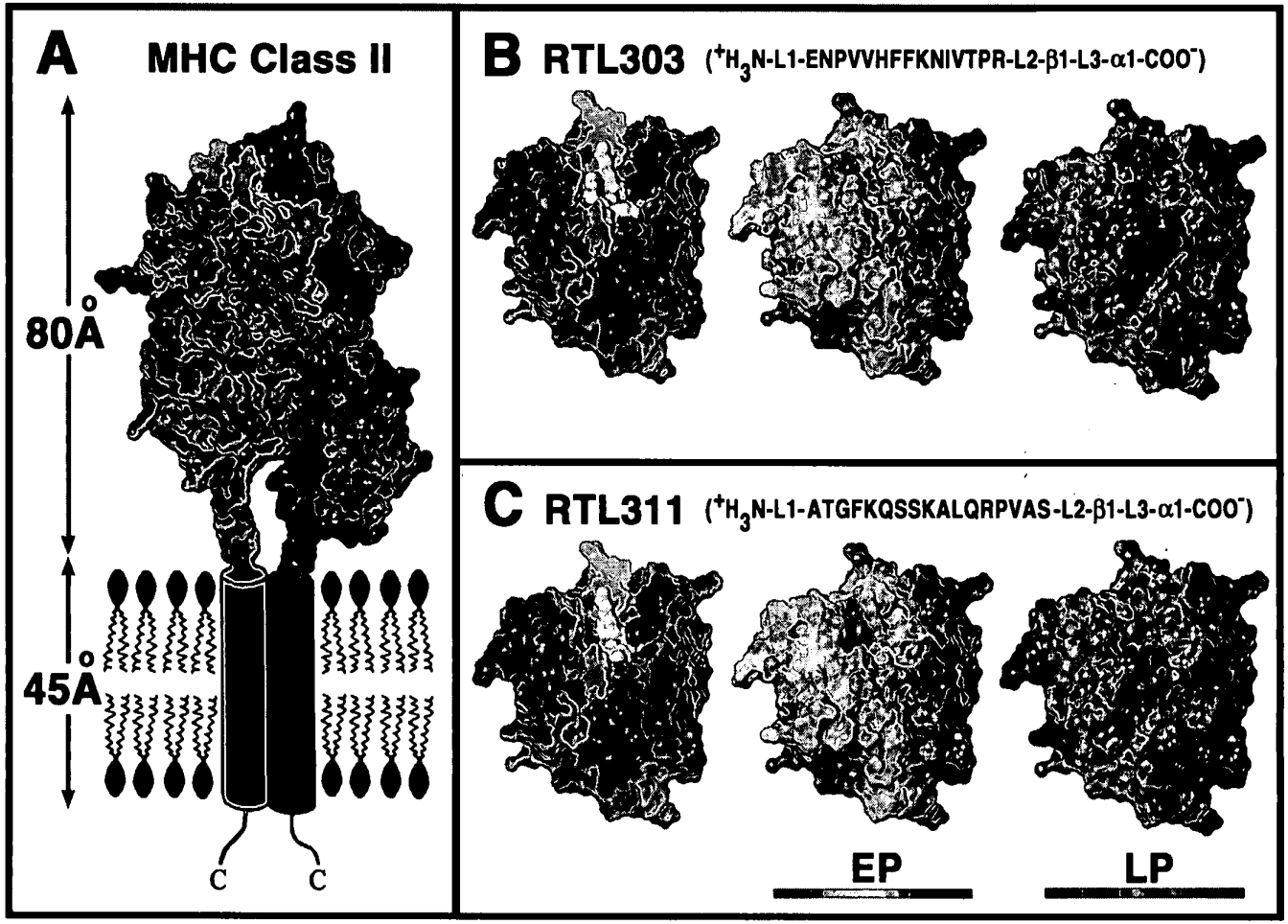

A
MHC Class II
80Å
45Å
C
C
B RTL303 (+H3N-L1-ENPVVHFFKNIVTPR-L2-β1-L3-α1-COO-)
C RTL311 (+H3N-L1-ATGFKQSSKALQRPVAS-L2-β1-L3-α1-COO-)
EP
LP

FIG. 19

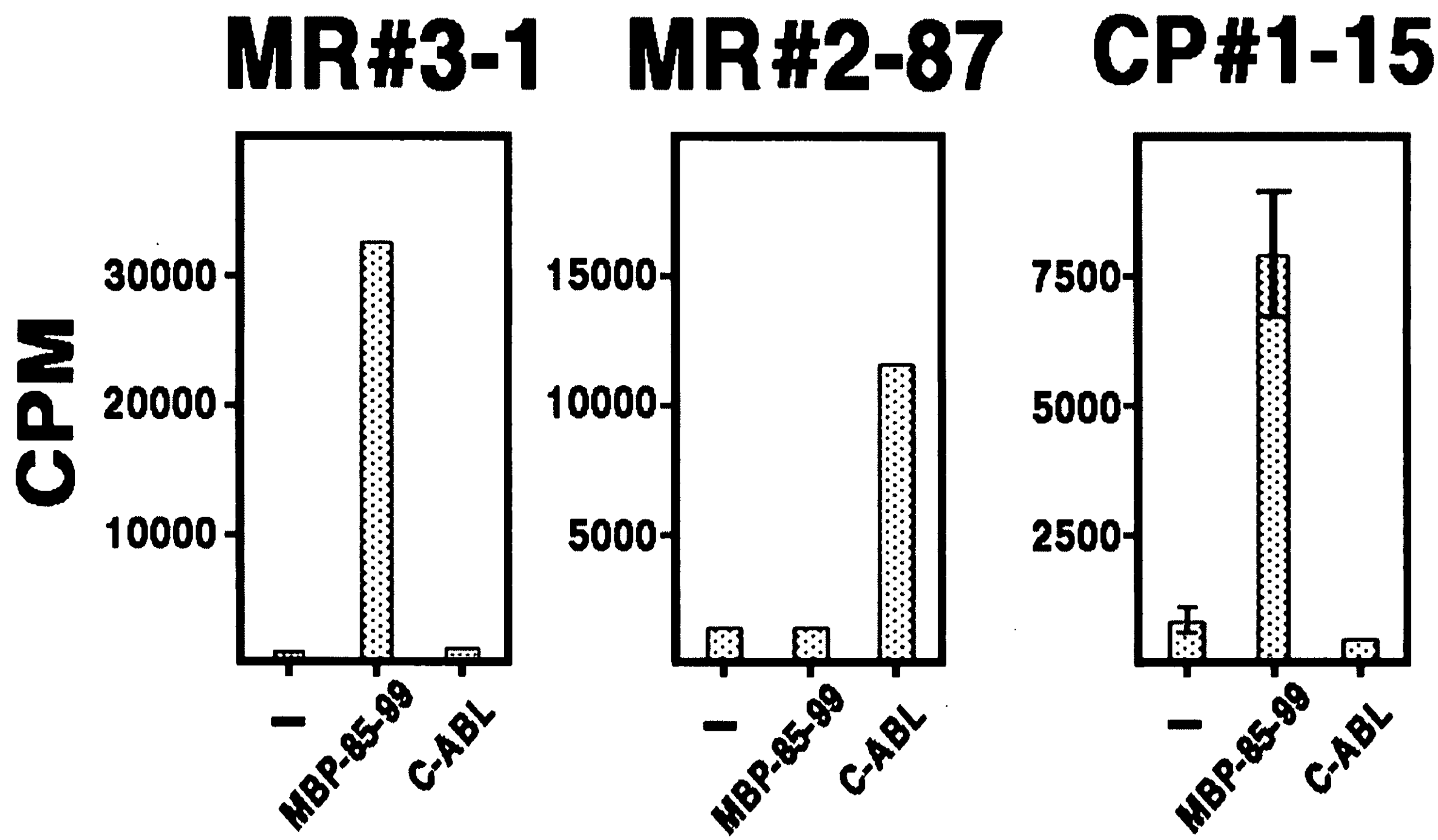

MR#3-1
MR#2-87
CP#1-15
CPM
30000
20000
10000
15000
10000
5000
7500
5000
2500
—
MBP-85-99
C-ABL

FIG. 20

FIG. 21 A

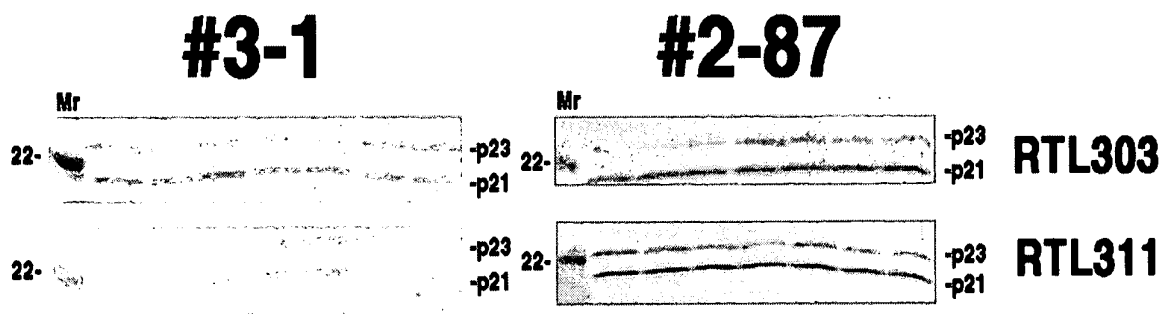
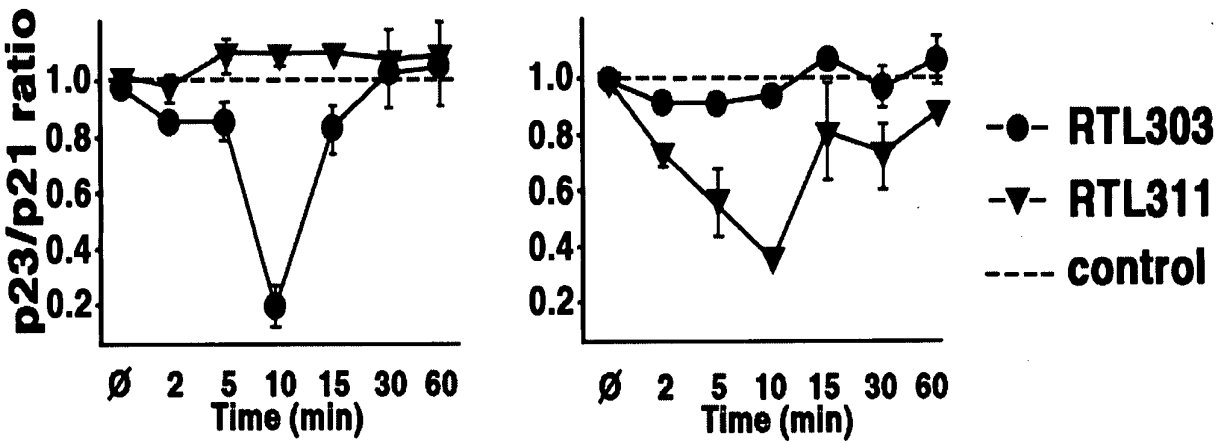


FIG. 21 B



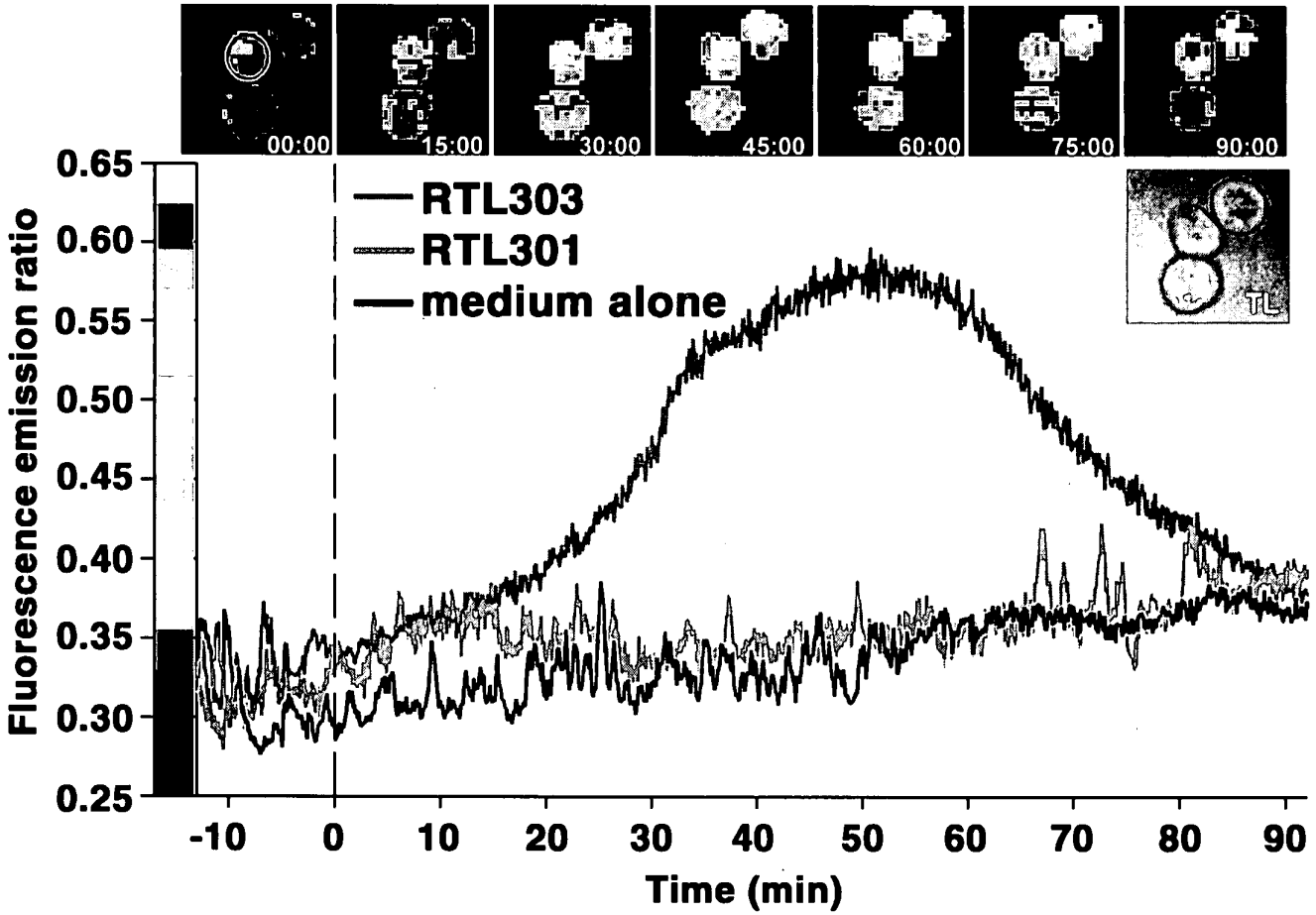


FIG. 22

FIG. 23 **A**

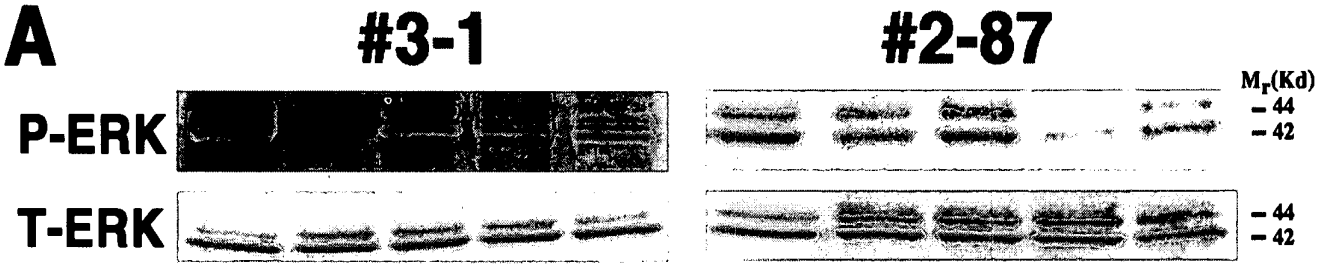


FIG. 23 **B**

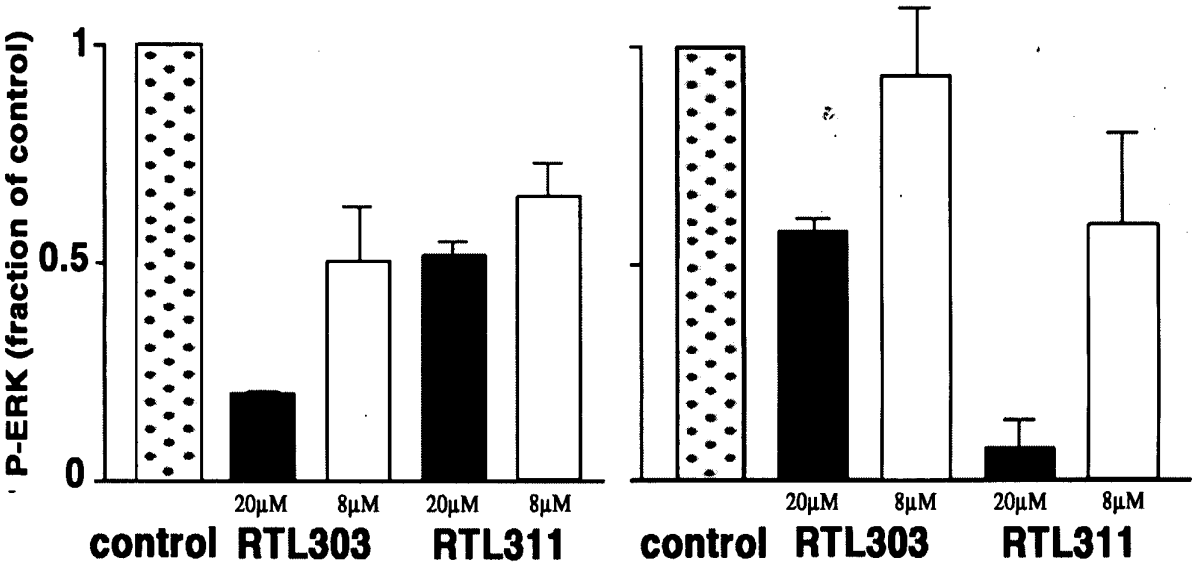


FIG. 24 **A** **MR#3-1**

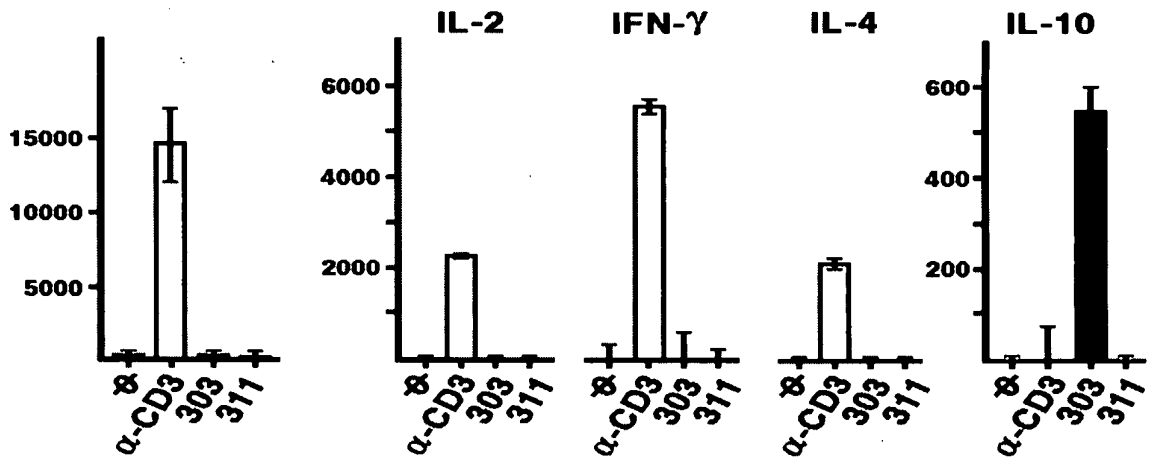


FIG. 24 **B** **MR#2-87**